

Global Rinderpest Eradication: Lessons Learned and Why Humans Should Celebrate Too

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Mota and Qaranyo, why are they not plowed?

... I came from there to here without seeing an ox...

-Line from Ethiopian poem
[1, 2], 1890s

After more than a decade of effort by the Global Rinderpest Eradication Programme (GREP) of the UN Food and Agricultural Organization (FAO), the Organisation mondiale de la santé (Office international des épizooties [OIE]), and the International Atomic Energy Agency (IAEA), among others [3–5], the veterinary disease rinderpest (Figure 1) was declared eradicated on 25 May 2011 [6]. Since rinderpest virus does not cause human disease, why is this achievement important to humans?

Since at least the Roman era, rinderpest (German for “cattle plague”) has been indirectly responsible for countless human deaths resulting from agricultural losses that led to famine and disease. The Ethiopian poem cited above refers to an

African rinderpest panzootic that caused rapid loss of virtually all of the cattle, buffaloes, elands, and wild swine, as well as many sheep, goats, and wildlife species, such as antelopes, gazelles, giraffes, hartebeest, and wildebeest (the “Great Ethiopian Famine” of 1887–1892 [2, 7–11]). Rinderpest virus (RPV) not only infects cattle but also infects >40 other domestic and wild artiodactyl species. It has been credited with decimation of native African wildlife species and even the decline of the European bison.

The Ethiopian tragedy exemplifies the importance of animal disease to humans. Without cattle to plow fields and fertilize crops with dung, the once-fertile Ethiopian lands became a graveyard. Planting and harvesting ceased; vast destruction of the native fauna and ecosystem led to a surge of crop-destroying rats and swarms of locusts and caterpillars likened at the time to a biblical plague [2]. Desperate for food, people first boiled and ate the skins of decomposed cattle, then abandoned their farms and villages to forage, consuming leaves and roots, picking through animal dung for undigested seeds, and eating the rotting corpses of horses, dogs, hyenas, jackals, and vultures. Some turned to cannibalism. Parents sold their children into slavery in the hope that slave masters would save the childrens’ lives by feeding them. Others committed suicide and murder. Smallpox epidemics broke

out. Starving people fell and died in the forests, along roadsides, and around churches. Lions, leopards, and jackals began to attack and kill people in broad daylight. Throughout the night, villagers heard the screams of starvation-weakened neighbors being dragged off and eaten by hyenas [2]. Speculative estimates of the human death toll in affected parts of East Africa reach as high as one-half to two-thirds of the population [2]. Some historians cite rinderpest as an ultimate cause of the Matabele War [9]. The last line of the poem (“I came from there to here without seeing an ox”) has a double meaning: “I came from there to here over dead bodies” [1, 2].

RPV is a single-stranded, negative-sense RNA virus of the family *Paramyxoviridae* (subfamily *Paramyxovirinae*, genus *Morbillivirus*) [12, 13]. The morbilliviruses are important pathogens of humans and animals and include human measles virus (MeV), peste-des-petits-ruminants virus, canine distemper virus, phocine distemper virus [14], and the cetacean morbilliviruses, including dolphin morbillivirus, porpoise morbillivirus, and pilot whale morbillivirus [15–19]. Additional morbilliviruses likely infect other animal species (eg, English hedgehogs [20]) and undoubtedly other species. Although peste-des-petits-ruminants-virus can also infect cattle and may be a target for future eradication efforts [21], the associated disease is subclinical;

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Figure 1. Cattle dead of rinderpest in the years after the devastating African rinderpest panzootic, which began in 1887. This photograph was probably taken around 1896 near Vryburg, Transvaal, South Africa (Veterinary History Society of Onderstepoort Veterinary Research Institute).

transmission between small ruminants and cattle is unlikely [22].

RPV transmission typically results from close contact with an infected animal via inhalation of virus-containing nasal, oral, or fecal secretions. Classical disease progression includes a silent incubation period lasting 8–11 days, prodromal fever, a mucosal phase beginning 4–5 days after fever onset, and a violent diarrheal stage lasting 1–2 days, followed by either dehydration and death or gradual recovery. Mortality rates approaching 100% have been documented, but milder forms of enzootic disease, attributed to stable strains of reduced virulence, sometimes cause mortality rates as low as 5%–10% [9, 23, 24].

Rinderpest has had a profound influence on public health. The 19th century devastation of Africa by rinderpest was preceded by a century of recurring European epizootics and panzootics that led to an estimated 20% loss of dairy cattle, undoubtedly retarding economic development and increasing poverty, malnutrition, and the infectious diseases that follow [25, 26]. Rinderpest is alleged to have been imported from Europe into the United States in the 1860s but did not become established [27, 28]. After a massive epizootic in 1709 [29–31],

programs to control rinderpest constituted one of Europe's major public health efforts. Rinderpest was the first infectious disease to be successfully controlled by active intervention; the techniques of restriction of animal movement, formation of *cordons sanitaires*, isolation, animal destruction, and disinfection [32, 33] were later applied to human diseases and became cornerstones of public health practice [26]. Rinderpest led to one of the earliest theories of infectious diseases [25, 26], one of the first plans to vaccinate (9 years before the 1720 European introduction of smallpox inoculation [10, 22]), the first demonstration of protective maternal immunity [34, 35], and one of the first uses of a thermometer to document febrile illnesses [36]. Long associated with war and natural disasters, RPV was one of the first infectious agents to be suspected as a bioweapon [2]. The ravages of rinderpest led directly to the establishment of the OIE in 1924.

Although it was initially unsuccessful, the development of rinderpest vaccine was among the earliest efforts of Robert Koch (1843–1910) and Sir Arnold Theiler (1867–1936). An attenuated goat-passaged vaccine was eventually developed in

the 1920s. After decades of public health efforts, Walter Plowright and colleagues developed a vaccine capable of eradicating RPV in the 1950s [37, 38]; it was modeled after the vaccine then being developed to prevent infection with the closely related MeV. For his pioneering work, Plowright was elected to the Royal Society in 1981 and was awarded the World Food Prize in 1999. Sadly, Plowright died in 2010, but he was aware that rinderpest eradication was imminent. Arnold Theiler's son Max (1899–1972) went on to develop the yellow fever vaccine, the first successful human live virus vaccine.

The eventual control of rinderpest with prevention measures and vaccines was not without consequences for African ecosystems. The rebound in the wildebeest population led simultaneously to marked decreases in the grasses and herbs they feed on and increases in predator species, such as lions [11]. After the deaths of so many wild and domestic artiodactyl hosts in parts of Africa, during the great 1890s rinderpest panzootic, the virus was paradoxically credited with elimination of the tsetse fly (*Glossinidae* species) and, consequently, the trypanosomal parasite responsible for African sleeping sickness [9]. These effects remind us that both the devastation of and

the control/eradication of infectious diseases in wildlife can have major, if unappreciated, ecological effects.

The evolutionary relationship between RRV and MeV is also noteworthy. Although the goal of eradicating measles remains unstated formally, aggressive efforts by the World Health Organization and many member nations have greatly reduced global measles deaths to the point where early steps toward eradication are now being taken [39–41]. Rinderpest, the second disease after smallpox to be eradicated, provides encouragement that measles can also soon be eradicated; the two diseases share such critical virologic and epidemiologic features as a single viral immunotype, few inapparent infections, lack of a chronic carrier state, and vaccine induction of long-standing protective immunity. That MeV has no extrahuman reservoir contributes further to its eradicability [42].

Phylogenetic analysis reveals that RRV is the closest relative of MeV, suggesting that RRV, or something very like it, gave rise to MeV [43]. Under this scenario, an ancestral RRV-like virus jumped to humans when humans started to domesticate cattle for agricultural purposes [9] and evolved into the infectious agent that we now know as MeV. However, because there is still a relatively large genetic distance between RRV and currently circulating MeV strains [44], it remains possible that an as-yet unsampled morbillivirus is the true ancestor of measles. However, despite the close contact between humans and cattle, and despite the past high prevalence of RRV in some geographical regions, there is no evidence that RRV symptomatically infects humans. Modern molecular biology has led to the discovery of a multitude of new viruses, including some new members of the *Paramyxovirinae* [45–49], although none are closer to MeV than RRV. If RRV is the ancestor of MeV, eradicating the ancestor of a human virus before eradicating the human virus itself would

certainly be a unique and ironic step in disease control.

It is quite likely that new morbilliviruses will be found as we sample more of the viral universe, some of which could conceivably jump species barriers to infect humans in the future [50]. In particular, the fact that modern-era intensive farming and mass animal transport have seemingly increased the likelihood of emergence of human diseases such as pandemic influenza, Nipah virus disease, salmonellosis, and bovine spongiform encephalopathy/variable Creutzfeldt-Jakob disease, should give us pause for thought. The story of rinderpest and its possible role in the genesis of measles should stimulate more research into how RNA viruses can jump species boundaries to infect new hosts [50, 51]. The 2000-year recorded history of rinderpest suggests to us that greater efforts should be placed on keeping the genie in the bottle rather than trying to put it back inside. Continued surveillance of human and animal populations for emerging morbilliviruses should clearly be a public health priority.

As rinderpest becomes the second eradicated infectious disease, saving not only countless animal and human lives but also the considerable expense of continuous control efforts, it is worth noting that, in addition to measles [39–41], two other human diseases are also close to eradication: polio [52, 53] and dracunculiasis [54]. In both cases, however, setbacks and delays have caused many to lose faith. The generation that eradicated smallpox is now handing off the baton of progress to a new generation, one that has come of age grappling with newly-emerging and re-emerging diseases, such as AIDS, severe acute respiratory syndrome, and pandemic influenza, but possessing powerful new research tools. The triumph of rinderpest eradication should challenge the current scientific generation to view disease eradication as the ultimate means of control and

prevention, to pursue eradication when the tools become available, and to seek to develop those tools when they are not available.

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